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L Number	Hits	Search Text	DB	Time stamp
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23	59	sophora and rhizoma	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/23 05:24
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26	1	rhizoma near4 discorea	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/23 05:25
28	0	rhizoma adj discorea	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/23 05:25
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36	4	(((424/725,757,773).CCLS.) and (diaper or wipe)) and sophora$	USPAT; US-PGPUB	2004/06/23 06:21

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38	0	sophora$ and wet adj wipe	USPAT; US-PGPUB	2004/06/23 06:22
39	6	sophora$ and towel$	USPAT; US-PGPUB	2004/06/23 06:28
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-	2	(("6149638") or ("6186991")).PN.	USPAT; US-PGPUB	2004/06/22 11:53
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-	97	sophora adj flavescens	EPO; DERWENT	2004/06/22 12:09
-	157	sophora adj flavescens	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/23 04:53
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-	0	(sophora adj flavescens) and diaper	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 12:10
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-	0	(diaper and plant adj extract) and flavescens	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 12:11
-	5	diaper and sophora	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 12:13
-	179	tissue and sophora	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 12:21
-	21	rash and sophora	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 12:22
-	1	(sophorae or sophora) and Discorea	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:11
-	1	Discorea adj Rhizoma	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 14:56
-	124	herb and diaper	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 14:56
-	24	wild adj yam adj root	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:19
-	0	(sophora adj flavescens) and (wild adj yam)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:01
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-	0	((wild adj yam) or (wild adj yam adj root)) and sophora	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:01
-	1315	sophora	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:18
-	1	sophora and discorea	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:02
-	59	sophora and rhizoma	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:10
-	1	(sophora and rhizoma) and discorea	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:10
-	108	wild adj yam	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:11
-	0	((sophorae or sophora) with flavescens) and discorea with rhizoma	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:14
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-	16	ku adj shen	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:15
-	0	sophora and (wild adj yam)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:19
-	0	sophora and (wild adj yam adj root)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:20
-	0	(ku adj shen) and (wild adj yam adj root)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 15:20
-	160	(sophorae or sophora) with flavescens	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/22 16:15

US006027728A

United States Patent [19]

Yuen

[11] Patent Number: 6,027,728

[45] Date of Patent: *Feb. 22, 2000

[54] **HERBAL SKIN REGENERATION COMPOSITION AND METHOD**

[76] Inventor: **Liu Yuen**, 534 E. Valley Blvd., #4, San Gabriel, Calif. 91777

[*] Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

[21] Appl. No.: **09/129,361**

[22] Filed: **Aug. 5, 1998**

[51] **Int. Cl.**[7] **A01N 65/00**

[52] **U.S. Cl.** **424/195.1**; 424/74; 514/783

[58] **Field of Search** 424/70.6, 74, 195.1, 424/450; 514/783

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Primary Examiner—Herbert J. Lilling

[57] **ABSTRACT**

The present invention comprises a selection of herbal materials with curative effects combined in a powdered form for application to human skin to accomplish skin regeneration, particularly for application to human skin affected with eczema, psoriasis, allergic reactions, inflammatory rash and the like. The process of application is critical to effectiveness of the present invention. The application of the herbal powder to the skin is intended to cause a temporary inflammation which removes at least an upper skin layer, with some mild to noticeable discomfort, and causes accelerated skin regeneration so that soft, unaffected skin replaces the scaling and/or lesioned skin.

3 Claims, No Drawings

HERBAL SKIN REGENERATION COMPOSITION AND METHOD

BACKGROUND OF THE INVENTION

The present invention relates to herbal skin regeneration compositions and methods of application to human skin to accomplish such skin regeneration, particularly for application to human skin affected with eczema, psoriasis, allergic reactions, inflammatory rash and the like.

Chinese medical arts rely heavily on compositions prepared and specially administered from among a relatively large selection of raw and processed herbal materials. The following are examples of such materials and applications related to human health, especially related to skin and connective tissue health.

The Panax family is known by its numerous varieties, the best known of which are as follows: *Panax ginseng* (C. A. Meyer), which is most frequently used for its medical attributes, *Panax notoginseng, Panax pseudo-ginseng* (subsp. *himalaicus*), *Panax japonicus* (var. major; var. *angustifolius*), *Panax quinquefolium, Panax trifolius, Panax zingiberensis* and *Panax stipuleanatus. Panax ginseng* seems to be among the most saponin-rich and the most effective. Panax originate essentially from Japan, China and Korea. The varieties cultivated in these different zones can be slightly different and are exposed to different geoclimatic conditions. Very different saponin contents are found in the different parts of the plant. The root part is the most frequently used and generally the most active. The highest saponin content is observed in the end of the root (ninjin in Japanese) and in the hairy roots (keninjin in Japanese). Planta Med. 1990, 56(1), 19–23, describes its use as an anti-inflammatory. As described in U.S. Pat. No. 5,747,538, ginsenoside R0 and plant extracts in which it is present have a stimulating activity on the synthesis of collagen, particularly collagens of types I and III, hereafter abbreviated respectively to "collagen I" and "collagen III".

Now, type I collagen represents 80 to 90% of the total skin collagen, the remainder, i.e. about 10 to 15% of the total skin collagen, consisting mainly of type III collagen. Type I and type III collagens are very intimately associated to form fibers within the dermis (BOREL J. P., MONBOISSE J. C., C. R. Soc. Biol. (1993), 187, 124–142; LAPERE C. M., Br. J. Dermatol. (1990), 122, 5–11).

Thus, irrespective of its origin, whether it be spontaneous as in the case of natural aging, or whether it be induced by a pathological condition, by drugs or by exposure to ultraviolet radiation, the decrease in the proportion of collagens I and III can be slowed down, or even stopped, by carrying out the process of U.S. Pat. No. 5,747,538 in order to stimulate collagen synthesis.

In addition, the article, "Research and development of cancer chemopreventive agents in China". J Cell Biochem Suppl. 1997; 27: 7–11, indicates that red ginseng, a processed *Panax ginseng*, is considered a typical tonic in traditional Chinese medicine. The studies demonstrated that red ginseng extract inhibited DMBA-induced skin papilloma significantly.

The genus Prunus (wild plum) has been reported to have skin-affective properties. In Biol Pharm Bull 1994 October 17(10):1417–1420, "Studies of cuticle drugs from natural sources. II. Inhibitory effects of Prunus plants on melanin biosynthesis", Matsuda H, Nakamura S, Kubo M, it was reported that the leaves of *P. zippeliana* inhibit melanin biosynthesis which is involved in hyperpigmentation and could be used as a whitening agent for the skin.

Some herbal preparations result in temporary skin inflammation. In Cutis 1993 June; 51(6):424, "Honeysuckle contact dermatitis", Webster R M, there is a case report and discussion of linear itchy raised blisters on the wrist of a patient that pulled Hall's Japanese honeysuckle (*Lonicera japonica holliana*). Also reported are results of antimicrobial action of flos Lonicera.

In Yakugaku Zasshi 1989 February; 109(2):113–118, "Studies on chemical protectors against radiation. XXVI. Protective effect of various extracts on crude drugs on skin injury induced by X-irradiation", Sato Y, Ohta S, Sakurai N, Shinoda M, the protective potency against skin injury on mice induced by X-irradiation was studied by use of 72 extracts of crude drugs. The protective potency was determined according to the degrees on skin injury after irradiation of 1100R, 30 k Vp soft X-ray. As a result of these study, 16 kinds of crude drugs such as *Rosae Fructus, Aloe arborescens* (*Herba*), *Citri Leiocarpae Exocarpium, Schizonepetae Spica, Evodiae Fructus, Bupleuri Radix, Corni Fructus, Perillae Herba, Anemarrhenae Rhizoma, Menthae Herba, Trapae Fructus, Angelicae Dahuricae Radix, Sinomeni Caulis et Rhizoma, Ephedrae Herba, Acer nikoense* (*Cortex*), *Forsythiae Fructus*, revealed protective potencies on skin injury.

Herba Taraxaci, common name dandelion, has been shown in use as a poultice of pulverized leaves mixed with dough applied to a bad bruise. Robbins W. W., J. P. Harrington and B. Freire-Marreco, 1916, "Ethnobotany of the Tewa Indians", Publication SI-BAE Bulletin #55, p. 61.

In the article, "Thermal and antiradical properties of indirect moxibustion", Am J Chin Med 1997; 25(3–4): 281–287, Chiba A, Nakanishi H, Chichibu S, the thermal and antiradical properties of indirect moxibustion stimulation were investigated by thermal qualitative and spectroscopic methods. The thermal effect of indirect moxibustion was mainly dependent on the spacing distance between the moxa and skin, and not on the moxa weight. The radical scavenging activities of moxa and moxa-tar were measured by a photometric absorbance method, chemical reaction with 1,1-diphenyl-2-picrylhydrazyl. The obtained results indicate that the inhibitory effects of moxa and moxa-tar on superoxide production are due to the radical scavenging mechanism.

In the article, "Main pharmacological roles and clinical curative effect of sanbi rebao", Chung Hsi I Chieh Ho Tsa Chih, 1990 September; 10(9):545–546, Zhao D K, Xu H Q, Liu J S, Sanbi Rebao (contain 32 components, such as *Radix Aconiti, Rhizoma Chuanxiong, Semen Strychni, Radix Glycyrrhizae, Radix Angelicae sinensis, Radix Ledebouriellae, Fructus Evodiae, borneolum syntheticum*, etc.) had antagonistic action on the ear swollen response induced by croton oil and on the ear inflammation reaction caused by dimethylphenylene in mice. It could decrease significantly the response rate of turning its body induced by acetic acid, increase the pain threshold caused by warm, reduce the surface seepage of injure skin and accelerate the wound recovery. The above results showed Sanbi Rebao possessed the roles of dephlogisticate, analgesia and promoting wound recovery, Besides these, clinic research indicated that effective rate of Sanbi Rebao on pain or numbness caused by cold, damp and wind (rheumatism) was 97%.

In the article "Clinical and experimental study of burns treated locally with Chinese herbs", Chung Hsi I Chieh Ho Tsa Chih 1991 December; 11(12):727–729, Wang G D, Zhang Y M, Xiong X Y, the authors decsribe selecting some traditional herbs to cure a burn wound, which had not only

the function of improving the local microcirculation of the burned surface and their bactericidal action, but also the function of changing the bacterial growth milieu action. *Coptis chinensis* 40%, *Herba Taraxaci* 40%, *Fructus Mume* 10% and *Salvia miltiorrhizae* 10% were boiled, infiltrated and disinfected. The mixture thus made was called as Burn II, which were applied on the burned surface daily, 97.1% of 103 patients were cured. Through the experiment of 60 rabbits burned by irons, which were divided into 6 groups (n=10 in each group) and each 2 groups infected respectively with *Bacillus pyocyaneus, Bacillus Coli* and *Staphylococcus Aureus*, took one of each infected group as control group. After 14 days, the infected burned surfaces which were applied with Burn II daily. The results showed that the effect of Burn II was not only significant, but also its usage was not highly restricted by the medical condition.

In the article "Inhibition of Na+,K(+)-ATPase by 1,2,3,4,6-penta-O-galloyl-beta-D-glucose, a major constituent of both *moutan cortex* and *Paeoniae radix*", Biochem Pharmacol 1997 February 21; 53(4):611–614, Satoh K, Nagai F, Ushiyama K, Yasuda I, Seto T, Kano I, the inhibition of Na+,K(+)-ATPase activity by various constituents of Moutan Cortex and *Paeoniae Radix* was studied. 1,2,3,4,6-Penta-O-galloyl-beta-D-glucose (PGG), a major component of both crude drugs, strongly inhibited Na+,K(+)-ATPase activity (IC50=2.5×10(−6) M), whereas galloylpaeoniflorin, benzoic acid, and catechin were weakly inhibitory, and albiflorin, oxypaeoniflorin, paeoniflorin, paconol, and phenol were ineffective. The inhibition of Na+,K(+)-ATPase activity by PGG was decreased in the presence of BSA or phospholipids. The inhibition mode of PGG was noncompetitive with respect to ATP. The K0.5 value for Na+ was increased by the addition of PGG from 9.1 to 12.3 mM, whereas that for K+ was not altered. PGG also inhibited K(+)-dependent p-nitrophenyl phosphatase activity with an IC50 value of 5.3×10(−6) M, and the extent of the inhibition increased at higher concentrations of K+. The K0.5 value for K+ was decreased by the addition of PGG from 3.3 to 2.0 mM. These results suggested that the inhibition of Na+,K(+)-ATPase activity is caused by interaction of PGG with the enzyme in the E2 state. The inhibitory effect of *Moutan Cortex* or *Paeoniae Radix* is considered to be mainly attributable to PGG.

In the article, "Research on hemostatic constituents in carbonized *Schizonepeta tenuifolia* Brig", Chung Kuo Chung Yao Tsa Chih 1993 September; 18(9):535–538, Ding N W, Kong L D, Wu H, Wang S L, Long Q J, Yao Z, Chen J, it has been shown that the fat soluble extract SeE from carbonized *Schizonepeta tenuifolia* has an obvious hemostatic action. In a given range of dose there is a significant linear correlation between the logarithms of its doses and the reciprocal of the bleeding and coagulating times in mice. Obvious hemostatic action was observed after mice had been administered in ip and po respectively for 0.5 h and 1 h. The hemostatic time of the former was 6 h and the latter 12 h. The LD50 of StE in po was 2.652+/−0.286 g/kg, while in ip 1.945 4/−0.207 g/kg.

In the article "Effect of the basidiomycete *Poria cocos* on experimental dermatitis and other inflammatory conditions", Chem Pharm Bull (Tokyo) 1997 March; 45(3):492–494, Cuellar M J, Giner R M, Recio M C, Just M J, Manez S, Rios J L, the hydroalcoholic extract from *P. cocos* was examined for oral and topical anti-inflammatory activities. It proved to be active against carrageenan, arachidonic acid, tetradecanoyl phorbol acetate (TPA) acute edemas, TPA chronic inflammation and oxazolone delayed hypersensitivity in mice. Two lanostane-type triterpenes were isolated and identified by spectroscopic methods as dehydrotumulosic and pachymic acids. Their ID50 on acute TPA edema was 4.7×10(−3) and 6.8×10(−4) mumol/ear, respectively.

The above are reprintings of abstracts available at the InterNet Web site of the National Center for Biotechnology Information with an address at "www.ncbi.nlm.nih.gov./htbin-post/query?" for access to MEDLINE's abbreviated database available to the public.

At the InterNet Web site with an address at "www.dmu.ac.uk/ln/cmn/current/0046.html", the following was reported "6. INTRODUCTION OF SOME FAMOUS CHINESE PATENT DRUGS (SERIES 6), ZhiKe PiPa TangJiang (Cough Syrup of Loquat Leaf), PRINCIPAL INGREDIENTS: Loquat leaf (*Folium Eriobotryae*), Platycodon root (*Radix Platydoci*), Stemona root (*Radix Stemonae*), Cogongrass rhizome (*Rhizoma Imperatae*), ACTIONS: Resolving phlegm and relieving cough. INDICATIONS: Dysfunction of the lung-qi, manifested as cough, difficult expectoration in abundance. It is often used clinically for the treatment of cough dueto common cold. ADMINISTRATION AND DOSAGE: To be taken orally, 5–10 ml each time, 3 times a day, half of the amount for children. PACKING: Syrup, 100 ml per bottle. MANUFACTURER: Fuzhou Traditional Chinese Pharmaceutical Factory 324 Xiateng Road, Fuzhou, FuJian Province, P.R. China".

The publication "The Treatment of Pediatric Eczema with Shu Feng Qu Shi Tang" by Zhan Nai-jun, Zhe Jiang Zhong Yi Za Zhi (Zhejiang Journal of Traditional Chinese Medicine), #6, 1994, p. 262, describes the action, in combination with several other herbal components, of *Fructus Kochiae Scopariae* (Di Fu Zi), as effective in the healing of a eczematic lesion after itching had been eliminated by another composition without that component.

SUMMARY OF THE INVENTION

The present invention comprises a selection of herbal materials with curative effects combined in a powdered form for application to human skin to accomplish skin regeneration, particularly for application to human skin affected with eczema, psoriasis, allergic reactions, inflammatory rash, skin ulceration scarring, several tineas (*tinea corporis, tinea unguium, tinea capitis, tinea pedis, tinea manuum, tinea cruris, tinea barbae, tinea versicolor, tinea oral, cutaneous candidosis*). Swollen, numb and sore extremities (hand and foot) have responded well with reduced symptoms with treatments according to the present invention.

The process of application is critical to effectiveness of the present invention. The application of the liquid extract of the herbal powder to the skin is intended to cause a temporary inflammation which removes at least an upper skin layer, with some mild to noticeable discomfort, and causes accelerated skin regeneration so that soft, unaffected skin replaces the scaling and/or lesioned skin.

The process of application requires that the powdered herbal materials are immersed in a mixture of boiling water and rice vinegar (about 3% acetic acid). The resulting liquid extract (which includes, as the term is used herein, substantial amounts of undissolved, albeit softened, vegetable matter), when cooled, is bathed or rubbed on the affected skin surface, preferably with a soft towel. This method of liquid extract preparation and application is preferably repeated 1–3 times per day. As used herein, a treatment course will comprise use of 5 separate acts of liquid extract preparation and application thereof. A mild case of skin

problems is treated with 1–3 treatment courses. The most serious and stubborn of skin problems will require up to 20 treatment courses.

Individually, the components of the skin regeneration powder have medicinal value and/or are reactive with human skin chemistries. The combination of these components has not been previously thought to produce a substantially complete and accelerated skin removal and regeneration with the treatment method described below.

It is apparent that the accelerated skin removal is somewhat related to inducing a chemical pseudo-"burn" on a patient's skin. The prior art does not indicate that the skin regeneration powder of the present invention would result in an initial pseudo-"burn" of the affected skin with just sufficient removal of the skin to avoid a permanent scar and thereafter to promote accelerated new skin generation from the lower dermal layers. The discomfort to the patient has been found to be at an acceptable level in view of the substantial healing benefits of the present invention. Long term healing without return of the prior skin condition has occurred in a number of treated patients.

DETAILED DESCRIPTION OF THE INVENTION

The following is a list of skin regeneration powder components and approximate weight percents for each component in the that skin regeneration powder:

Component Name	Weight Percent
Prunus Mume Sieb	2.0
Cortex Dictamniradisis	2.0
Herba Menthae	5.0
Encedanium Regidum	2.0
flos Lonicerae	8.0
Radix Angelicae Pubescentis	2.0
Herba Taraxaci	4.0
Radix Stemonae	3.0
Alum	8.0
Herba Schizonepetae	6.0
Cortex Poria	3.0
Korean Red Ginseng	3.0
Di Fu Zi	5.0
Wu Zu Yu	6.0
Tribulus Terrestris	3.0
Fructus Cnidii	5.0
Radix Ledebouriellae	5.0
Radix Clematidis	5.0
Herba Moxa	3.0
Periostracum Cicadae	5.0
Radix Paenoniae Rubra	3.0
Sophora Flavescens Aiton	6.0
Asarum Chinese Wild Ginger	6.0
	100.0

It will be appreciated to those skilled in this art that the above approximate weight percents are dependent on generally expected potencies of the components, whereby the relative weight percents will vary sometimes substantially from the above individual amounts. It will be within the skilled person's knowledge with this disclosure that the objects of the present invention require the inclusion of each of the components in relative approximate weight percents above. As disclosed in the prior art, individual components comprise medicinal effects on the epidermis and dermis and are further comprise substantially absorbable molecular classes. Subgroups within the above list comprise those components which have similar known effects, i.e., some components have been shown to have substantial skin regeneration effects while others comprise skin irritant and/or astringent effects.

The above components are ground to a powder form well known in the Chinese herbal art. Such grinding may be accomplished manually with the components separately ground or ground together. The powder mixture is preferably substantially finer than 100 mesh. Each of the components in the above ranges is required to obtain the objects of the present invention.

A solution of a single liquid extract contains approximately 112 grams (dry weight) of the ground powder. The dry powder is placed in a boiling liquid of about 7.5 liters of water and one liter of rice vinegar and allowed to extract components of the powdered components by continued immersion throughout the subsequent cooling and application process. The length of time for extraction will necessarily depend on a desired strength of the extract liquid, although an extraction time of at least 5 minutes is required. The resulting extract liquid will have taken on a light brown color. The density and viscosity of the extracted liquid will be about the same as that of water.

This extract liquid is slightly acidic and comprises a highly complex mixture medicinally active molecules from the powdered components. The extract liquid must be used immediately upon cooling to a temperature just acceptable to the patient. It is believed from the relative lack of effectiveness of the extract liquid after about two hours that a continuing set of reactions occurs among the medicinally effective extracted molecules.

For the application steps, it is preferred that the extract liquid is retained in contact and in the same container in which the boiling extraction takes place. The extract liquid is absorbed into a towel or similar liquid absorbing material and applied to the affected skin area by rubbing at least about 20 minutes and more preferably about 30 minutes, refreshing the extract liquid in the liquid absorbing material about every minute. The application to the affected skin must be relatively softly, preferably by hand and with some gentle soaking of the affected area, although the degree of physical abrasion with the application cloth is determined primarily by the amount of callous in the affected area, i.e., the palm of the hand and soles of the feet will be rubbed at least gently and the face is only bathed without rubbing. The affected area must be washed with water after each application is complete. The treated area is then preferably dried and optionally covered with a tinea plaster and/or antiphlogistine. A light protective bandaging or covering is preferred between applications at the affected area, as emerging skin layers may be exposed to infection, as burn patients often are substantially exposed to substantial air-borne infection risk as new tissue develops in the burned area.

The patient will experience a mild to substantial burning sensation on application of the extract liquid, perhaps extending to a mild pain at the application area. Practice indicates that the discomfort is bearable for the patient with careful attention to the amount and strength of extract liquid applied to the affected skin area. After a single treatment course of five sets of extract liquid preparation and application at the rate of 1–3 sets of such extract liquid preparation and application per day, the patient must wait at least 34 days. The affected skin area in that 3–4 day period will become substantially reddened beneath an overlay of scaling and flaking skin.

Where the skin problems have persisted for 3–5 years, experience indicates that 3–5 treatment courses will be required to substantially eliminate the problem skin from

re-emerging. Where the skin problems have persisted for 10–20 years, experience indicates that up to 20 treatment courses will be required to substantially eliminate the problem skin from re-emerging.

The extract liquid is absorbed into the skin and to some extent into the connective tissue beneath it. It is highly recommended that the patient reduce or eliminate absorbable skin contact with alkali fluids or such foods and drink that promote a relatively basic blood chemistry. Some foods that the patient should avoid are shellfish, beef and fruits such as mango.

The extract liquid should never be taken internally or around the eyes. The extract liquid is to be used with extreme care, preferably not at all, by those with very sensitive skin, lupus erythematosus, scarlet fever or other such skin affective diseases, wounds or pregnant women. Because some skin bleaching is accomplished with the extract liquid, those with darker skin pigments should not use the extract liquid unless with the acceptance that affected area after treatment with the method of the present invention will be regenerated with substantially lighter skin.

The above composition and methods present the skilled person with considerable and wide ranges from which to choose appropriate obvious modifications for the above examples. However, the objects of the present invention will still be obtained by the skilled person applying such disclosures in an appropriate manner.

I claim:

1. A skin regeneration powder comprising, according to the following list by approximate weight percents:

Prunus Mume Sieb at about 2.0%;
Cortex Dictamniradisis at about 2.0%;
Herba Menthae at about 5.0%;
Encedanium Regidum at about 2.0%;
flos Lonicerae at about 8.0%;
Radix Angelicae Pubescentis at about 2.0%;
Herba Taraxaci at about 4.0%;
Radix Stemonae at about 3.0%;
Alum at about 8.0%;
Herba Schizonepetae at about 6.0%;
Cortex Poria at about 3.0%;
Korean Red Ginseng at about 3.0%;
Di Fu Zi at about 5.0%;
Wu Zu Yu at about 6.0%;
Tribulus Terrestris at about 3.0%;
Fructus Cnidii at about 5.0%;
Radix Ledebouriellae at about 5.0%;
Radix Clematidis at about 5.0%;
Herba Moxa at about 3.0%;
Periostracum Cicadae at about 5.0%;
Radix Paenoniae Rubra at about 3.0%;
Sophora Flavescens Aiton at about 6.0%; and
Asarum Chinese Wild Ginger at about 6.0%.

2. An aqueous, slightly acidic liquid extract from a skin regeneration powder, the powder comprising according to the following list by approximate weight percents:

Prunus Mume Sieb at about 2.0%;
Cortex Dictamniradisis at about 2.0%;
Herba Menthae at about 5.0%;
Encedanium Regidum at about 2.0%;
flos Lonicerae at about 8.0%;
Radix Angelicae Pubescentis at about 2.0%;
Herba Taraxaci at about 4.0%;
Radix Stemonae at about 3.0%;
Alum at about 8.0%;
Herba Schizonepetae at about 6.0%;
Cortex Poria at about 3.0%;
Korean Red Ginseng at about 3.0%;
Di Fu Zi at about 5.0%;
Wu Zu Yu at about 6.0%;
Tribulus Terrestris at about 3.0%;
Fructus Cnidii at about 5.0%;
Radix Ledebouriellae at about 5.0%;
Radix Clematidis at about 5.0%;
Herba Moxa at about 3.0%;
Periostracum Cicadae at about 5.0%;
Radix Paenoniae Rubra at about 3.0%;
Sophora Flavescens Aiton at about 6.0%; and
Asarum Chinese Wild Ginger at about 6.0%.

3. A method for skin regeneration comprising:

(a) preparing a liquid extract from a skin regeneration powder comprising, according to the following list by weight percents:
Prunus Mume Sieb at about 2.0%;
Cortex Dictamniradisis at about 2.0%;
Herba Menthae at about 5.0%;
Encedanium Regidum at about 2.0%;
flos Lonicerae at about 8.0%;
Radix Angelicae Pubescentis at about 2.0%;
Herba Taraxaci at about 4.0%;
Radix Stemonae at about 3.0%;
Alum at about 8.0%;
Herba Schizonepetae at about 6.0%;
Cortex Poria at about 3.0%;
Korean Red Ginseng at about 3.0%;
Di Fu Zi at about 5.0%;
Wu Zu Yu at about 6.0%;
Tribulus Terrestris at about 3.0%;
Fructus Cnidii at about 5.0%;
Radix Ledebouriellae at about 5.0%;
Radix Clematidis at about 5.0%;
Herba Moxa at about 3.0%;
Periostracum Cicadae at about 5.0%;
Radix Paenoniae Rubra at about 3.0%;
Sophora Flavescens Aiton at about 6.0%; and
Asarum Chinese Wild Ginger at about 6.0%;

(b) applying the liquid extract to a skin surface for about more than 20 minutes;

(c) repeating steps (a) and (b) at least four times; and

(d) withholding exposure of the skin surface to the extract liquid for about at least three days.

* * * * *

US005753242A

United States Patent [19]

Nakamura et al.

[11] Patent Number: 5,753,242

[45] Date of Patent: May 19, 1998

[54] **EXTERNAL SKIN TREATMENT COMPOSITION**

[75] Inventors: **Fumiaki Nakamura; Yoshimaru Kumano; Kenzo Ito**, all of Yokohama, Japan

[73] Assignee: **Shiseido Company, Ltd.**, Tokyo, Japan

[21] Appl. No.: **712,293**

[22] Filed: **Sep. 11, 1996**

Related U.S. Application Data

[62] Division of Ser. No. 468,504, Jun. 6, 1995, abandoned, which is a continuation of Ser. No. 250,143, May 27, 1994, abandoned.

[30] **Foreign Application Priority Data**

May 2, 1994 [JP] Japan 6-93500

[51] **Int. Cl.**[6] **A61K 7/00**

[52] **U.S. Cl.** **424/401**; 514/844

[58] **Field of Search** 424/401; 514/844, 514/848

[56] **References Cited**

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Primary Examiner—Gollamudi S. Kishore

Attorney, Agent, or Firm—Sprung Kramer Schaefer & Briscoe

[57] **ABSTRACT**

An external skin treatment composition comprising erythritol, hydrogenated lecithin, and a polyoxyethylene-added cholesterol derivative, which is superior in prevention and improvement of skin roughness, with little sticky feeling, with quick absorption into the skin, and superior in the softening effect on the corneum.

12 Claims, 1 Drawing Sheet

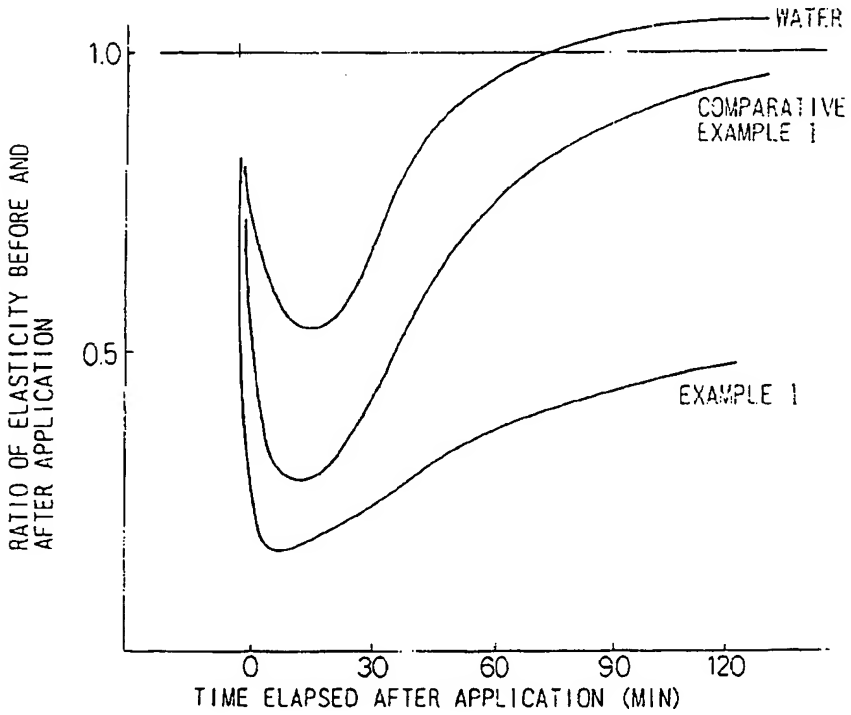
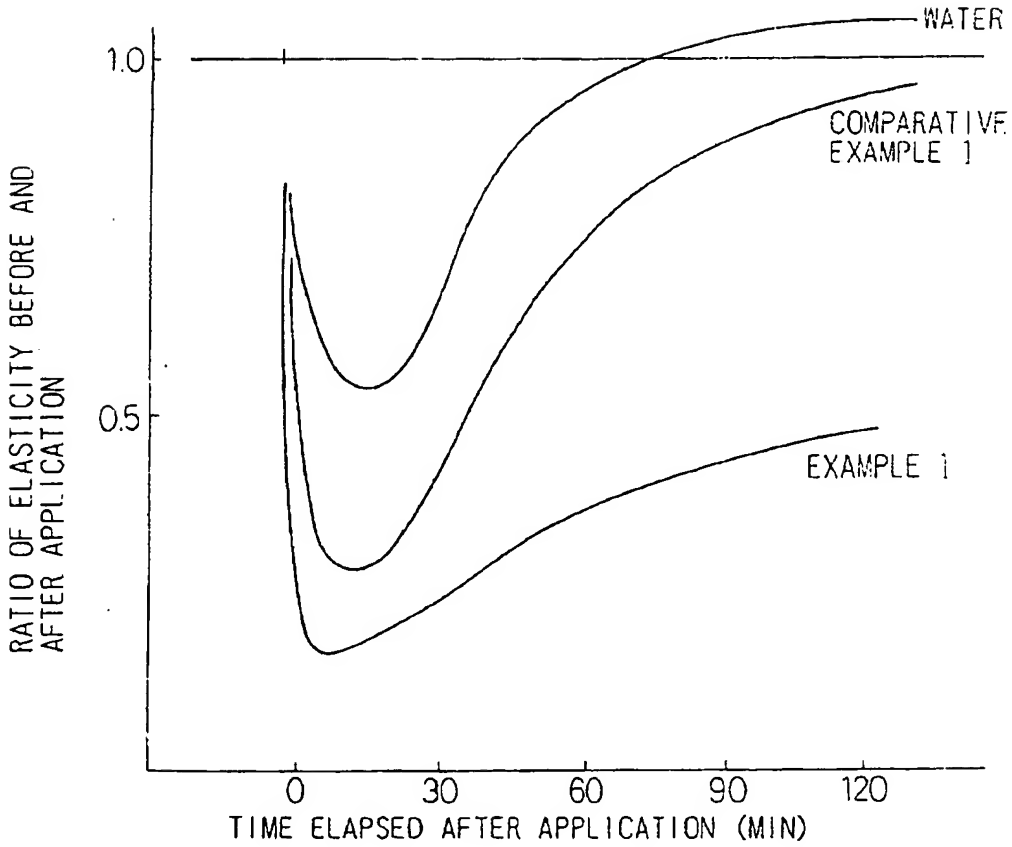


Fig.1


WATER
COMPARATIVE EXAMPLE 1
EXAMPLE 1
1.0
0.5
RATIO OF ELASTICITY BEFORE AND AFTER APPLICATION
0
30
60
90
120
TIME ELAPSED AFTER APPLICATION (MIN)

EXTERNAL SKIN TREATMENT COMPOSITION

This is a division of application Ser. No. 08/468,504, filed Jun. 6, 1995 now abandoned, which is a continuation of application Ser. No. 08/250,143, filed on May 27, 1994 now abandoned.

FIELD OF THE INVENTION

The present invention relates to an external skin treatment composition which improves skin roughness, is quickly absorbed into the skin, softens the stratum corneum, and is superior in a moisturizing effect.

DESCRIPTION OF THE RELATED ART

One of the main purposes of external skin treatment compositions such as cosmetics is the prevention and improvement of skin roughness. To achieve this purpose, in the past the practice has been to formulate various humectants such as glycerol, sorbitol, propylene glycol, polysaccharides.

However, there is the problem that humectants such as polysaccharides, precipitate in formulations with large alcohol contents. Glycerol, sorbitol, propylene glycol, chondroitin sulfuric acid, and the like cause stickiness and a burning sensation when formulated in too much. In the case of amino acids such as DL-threonine cause the problems of discoloration or generation of foreign odors.

SUMMARY OF THE INVENTION

Accordingly, the objects of the present invention are to eliminate the above-mentioned problems of the conventional external skin treatment composition and to provide an external skin treatment composition capable of improving skin roughness, of being quickly absorbed into the skin, of softening the stratum corneum and of being superior in moisturizing effect.

Other objects and advantages of the present invention will be apparent from the following description.

In accordance with the present invention, there is provided an external skin treatment composition comprising erythritol, hydrogenated lecithin, and a polyoxyethylene-added cholesterol derivative.

BRIEF DESCRIPTION OF THE DRAWING

The present invention will be better understood from the description set forth below with reference to the accompanying FIG. 1, which is a graph showing the results of measurement of the softening effect on the stratum corneum by the external skin treatment composition according to the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present inventors, in consideration of the above situation, engaged in repeated in-depth studies and as a result found that an external skin treatment composition composed of a mixture of erythritol, hydrogenated lecithin, and a polyoxyethylene-added cholesterol derivative not only is superior in the prevention and improvement of skin roughness, but also is small in the stickiness observed in the case of in glycerol, sorbitol, and other polyhydric alcohols, is quickly absorbed into the skin, and is superior in the softening effect of the stratum corneum and thus completed the present invention.

The present invention will now be explained in further detail.

The erythritol usable in the present invention is also called meso-erythritol and is a sugar alcohol of tetrasaccharide contained in liche, basidium, fruit, and the like in the natural world.

The amount of the erythritol formulated in the present invention is preferably 0.1 to 30% by weight based on the weight of the external skin treatment composition, more preferably 0.5 to 20% by weight. When this amount is less than 0.1% by weight, the effect of improving skin roughness and moisturization is difficult to obtain. Conversely, when the amount is more than 30% by weight, no further increase can be expected in the effect of improvement of skin roughness and moisturization.

The hydrogenated lecithins usable in the present invention are, for example, phospholipids extracted from egg yolk, soybeans, corn, rapeseed, etc. and hydrogenated by a conventional method. However, to obtain white, odorless, good quality lecithin by hydrogenation, it is necessary to use lecithin which has not been oxidized or brownized when hydrogenized.

The amount of the hydrogenated lecithin to be formulated in the present invention is preferably 0.0001 to 1% by weight, based on the weight of the external skin treatment composition, more preferably 0.0005 to 0.5% by weight. With an amount less than 0.0001% by weight, the quickness of absorption into the skin and the effect of softening the stratum corneum are difficult to obtain. Conversely, when the amount is more than 1% by weight, no further increase can be expected in the quickness of absorption into the skin and the effect of softening the stratum corneum.

As the polyoxyethylene-added cholesterol derivative usable in the present invention, mention may be made of polyoxyethylene-added cholestanolether, polyoxyethylene-added phytosterolether, etc. The preferable addition mole, number of the polyoxyethylene is 5 to 70 moles. Especially, the use of polyoxyethylene (30 mole added) cholesterol is most preferable in view of the effect.

The amount of the polyoxyethylene-added cholesterol derivative formulated in the present invention is preferably 0.0001 to 1% by weight, more preferably 0.0005 to 0.5% by weight, based on the weight of the external skin treatment composition. When the amount is less than 0.0001% by weight, the quickness of absorption into the skin and the effect of softening the stratum corneum are difficult to obtain. Conversely, when the amount is more than 1% by weight, no further increase can be expected in the quickness of absorption into the skin and the effect of softening the stratum corneum.

The external skin treatment composition of the present invention may include, in addition to the above-mentioned essential components, other ingredients generally used in the other cosmetics, pharmaceuticals, and other external skin treatment compositions so long as the desired effects of the present invention are not impaired.

As such ingredients, it is possible to formulate, for example, powder components such as titanium dioxide, mica, and talc, oils such as avocado oil, macademia nut oil, corn oil, olive oil, rapeseed oil, evening primrose oil, castor oil, sunflower oil, tea seed oil, rice bran oil, jojoba oil, cacao fat, palm oil, squalene, squalane, beef tallow, Japanese tallow, beeswax, candelila wax, carnauba wax, spermiceti, lanolin, silicone oil, liquid paraffin, ceresine, and vaseline, higher alcohols such as capryl alcohol, lauryl alcohol, myristyl alcohol, cetyl alcohol, and phytosterol, higher aliphatic

acids such as capric acid, lauric acid, myristic acid, palmic acid, stearic acid, behenic acid, lanolin fatty acid, linoleic acid, and linolenic acid, UV absorbents such as paraamino benzoic acid, homomenthyl-7N-acetyl-alantolanylate, butylmethoxydibenzoylmethane, di-p-methoxycinnamic acid-mono-2-ethylhexanoic acid glyceryl, amylsalicylate, octylmethoxycinnamate, and 2-hydroxy-4-methoxybenzophenone, moisture retainers such as polyethylene glycol, glycerol, sorbitol, xylitol, maltitol, mucopolysaccharide, hyaluronic acid, chondoroitin sulfate, and chitosan, thickeners such as methylcellulose, ethylcellulose, arabia gum, polyvinylalcohol, montmorillonite, and laponite, organic solvents such as ethanol and 1,3-butylene glycol, anti-oxidants such as butylhydroxytoluene, tocopherol, and phytic acid, antibacterial preservatives such as benzoic acid, salicylic acid, sorbic acid, alkyl esters of p-oxybenzoic acid (ethylparabene, butylparabene, etc.), and hexachlorophene, amino acids such as glycine, alanine, valine, leucine, serine, threonine, phenylalanine, tyrosine, asparagic acid, asparagine, glutamine, alginine, and hystidine and alkali metal salts thereof and hydrochlorides thereof, organic acids such as acylsarcosinic acid (for example, lauroylcosin sodium), glutathione, citric acid, malic acid, tartaric acid, and lactic acid, vitamin B's such as vitamin A and its derivatives, vitamin B_6 hydrochloride, vitamin B_6 tripalmitate, vitamin B_6 dioctanoate, vitamin B_2 and its derivatives, vitamin B_{12}, and vitamin B_{15} and its derivatives, vitamin C's such as ascorbic acid, ascorbic acid sulfate (salts), ascorbic acid phosphate (salts), and ascorbyl dipalmitate, vitamin E's such as α-tocopherol, β-tocopherol, γ-tocopherol, vitamin E acetate, and vitamin E nicotinate, vitamin D's, vitamin H, vitamins such as pantotenic acid and pantetine, drugs such as nicotinic acid amide, nicotinic acid benzyl, γ-oryzanol, alantoin, glycyrrhizic acid (salts), glycyrrhetiric acid and its derivatives, hinokitiol, musidine, bisabolol, eucalyptol, thymol, inositol, saponins (saikosaponin, ginseng saponin, dishcloth gourd saponin, mukuro disaponin), pantothenylethylether, ethynylestradiol, tranexamic acid, cepharantine, and placenta extract, organic solvents for rumex japonicus, sophora flavescens, nupharis rhizoma, orange, sage, milfoil, mallow, cnidium rhizome, swertia herb, thyme, Japanese angelica root, bitter orange peel, birch, field horsetail, dishcloth gourd, horse chestnut, creeping saxifrage, arnica, lily, mugwort, herbaceous peony, aloe, Cape jasmine, and saware cypress; natural extracts extracted by alcohol, polyhydric alcohols, water, aqueous alcohols, etc., dyes, nonionic surface active agents such as sorbitan monolaurate, sorbitan monopalmitate, sorbitan sequioleate, sorbitan trioleate, polyoxyethylene sorbitan monolaurate, polyoxyethylene sorbitan monostearate, polyethylene glycol monooleate, polyoxyethylene alkyl ether, polyglycol diester, lauroyl diethanol amide, aliphatic acid isopropanol amide, maltitol hydroxy aliphatic ether, alkylated polysaccharides, alkyl glucoside, and sugar esters, cationic surface active agents such as stearyltrimethyl ammonium chloride, chloride benzalconium, and laurylamine oxide, anionic surface active agents such as sodium palmitate, sodium laurate, sodium laurosulfate, potassium laurosulfate, alkyl sulfuric acid triethanolamine ether, scopolia oil, linear dodecylbenzene sulfonate, polyoxyethylene hydrogenated castor oil malonate, acylmethyltaurine, bipolar surface active agents, perfumes, purified water, etc.

The external skin treatment compositions of the present invention can include, for example, a preparation such as cosmetics, pharmaceuticals, and quasi-drugs which are applied to the external skin and accordingly may take the form of any preparation and a wide variety of types such as an aqueous solution type, a soltibilized type (for example, lotion), an emulsion type (for example, an emulsion or cream), a powder type (for example, a foundation), a dispersion type, an oil-in-water type, a gel, an application, a two-layer water and oil type, a two-layer water and powder type, or a three-layer water, oil, and powder type.

EXAMPLES

The present invention will now be further illustrated by, but is by no means limited to, the following Examples.

Example 1

Component	% by weight
Erythritol	10
Hydrogenated lecithin	0.5
Polyoxyethylene (30) cholestanolether	0.5
Water	89

(Method of Production)

A 100 g amount of erythritol, 5 g of hydrogenated lecithin, and 5 g of polyoxyethylene (30) cholestanolether were dissolved in warm water, followed by adding water to give a total weight of 1000 g.

Comparative Example 1

Component	% by weight
Erythritol	10
Water	90

Comparative Example 2

Component	% by weight
Hydrogenated lecithin	0.5
Polyoxyethylene (30) cholestanolether	0.5
Water	99

Evaluation Example

The moisture retention effect, quickness of absorption into the skin, softening effect on corneum, and skin improving effect of an aqueous solution of erythritol, hydrogenated lecithin, and polyoxyethylene (30) cholestanolether (Example 1), an aqueous solution solely containing erythritol (Comparative Example 1), and an aqueous solution of hydrogenated lecithin and polyoxyethylene (30) cholestanolether (Comparative Example 2) were compared.

Measurement of Moisture Retention Effect by Moisture Evaporation Rate

As the test for measuring the moisture retention effect, measurement of the moisture evaporation rate is suitable. That is, 10 μl of a sample solution is dropped on 2.0×2.0 cm filter paper, then the reduction in weight is measured every minute until the 10th minute and the reduction in weight per minute is found. As a control, use was made of distilled water. Note that the value of the moisture evaporation rate for water was made "1".

The results are shown in Table 1. As clear from the results of Table 1, the synergistic effect was observed by the

combination of erythritol, hydrogenated lecithin, and polyoxyethylene (30) cholestanolether according to the present invention.

TABLE 1

Moisture Evaporation Rate

Sample	Moisture evaporation rate
Water	1.00
Comparative Example 1	0.90
Comparative Example 2	0.98
Example 1	0.83

Measurement of Absorption into Skin

As the test for measuring the skin absorption effect, measurement of the contact angle with the skin is suitable. That is, 5 μl of a sample was dropped on the skin, then the angle between the drops and the skin (contact angle) after three minutes was measured. The results are shown in Table 2. As shown in Table 2, the absorption was observed to be improved.

The sample was the same type as that used for the measurement of the moisture retention effect.

TABLE 2

Absorption into Skin

Sample	Contact angle
Water	105°
Comparative Example 1	103°
Example 1	51°

Measurement of Softening Effect on Stratum Corneum

The softening effect on the stratum corneum was measured by coating 2 μl of an aqueous test solution on a 20 mm×5 mm corneum piece and then measuring the elasticity using a dynamic viscoelasticity measurement apparatus made by Toyo Seiki. The softening effect was expressed by the ratio Et/E of the elasticity at the time t after coating of the aqueous test solution with respect to the elasticity (E) of the corneum measured as the control.

The results are shown in FIG. 1.

As is clear from FIG. 1, the softening effect on the corneum is also increased by the combination of erythritol, hydrogenated lecithin, and polyoxyethylene (30) cholestanolether according to the present invention.

Action of Preventing Skin Roughness Caused by Application of Sodium Dodecyl Sulfate

Next, a test was made on erythritol and glycerol, which have a moisture retention effect, to determine their action of preventing skin roughness with respect to stimulus caused by sodium dodecyl sulfate. That is, the skin at the inside of the lower arms of 10 health male subjects was treated with a 3% aqueous solution of sodium dodecyl sulfate to cause skin roughness. After 2 hours, 40 μl of each of the samples was coated and maintained in an open state. The skin roughness was caused and samples coated repeatedly over five days. On the sixth day, the state of the skin roughness was visually measured. The evaluation criteria are shown in Table 3 and the results are shown in Table 4.

TABLE 3

Criteria for Evaluation of Skin Roughness

Score	Evaluation	Remarks
1	Drying of wide range of corneum, peel-of, and strong erythema are observed.	Rough skin
2	Drying of corneum, peel-of, and medium degree of erythema are observed.	↑
3	Drying of corneum can be observed, but no peel-of. Weak erythema are observed.	
4	No drying of corneum and peel-of can be observed, but some erythema are observed.	↓
5	No drying of corneum, peel-of, or erythema can be observed.	Beautiful skin

The judgement was made using the average value of the scores for 10 subjects.

Judgement of Skin Roughness

Excellent: Average score is from 4 to 5

Good: Average score is from 3 to less than 4

Fair: Average score is from 2 to less than 3

Poor: Average score is from 1 to less than 2

TABLE 4

Action for Preventing Skin Roughness

Sample	Action preventing skin roughness
Water	Poor
10% glycerol	Good
Comparative Example 1	Good
Example 1	Excellent

In the above way, a skin roughness preventing action is observed in both glycerol and erythritol, but it is clear that the synergistic effect is exhibited by combination of hydrogenated lecithin and polyoxyethylene (30) cholestanolether with erythritol.

Test of Actual Use

The results of improvement of skin roughness according to a test of actual use are shown below:

Test Method

The surface conditions of the skin of healthy female subjects (face) were observed by under a microscope (17X) by taking replicas of the skin using the silicone resin replica method. That is, use was made of a group of 30 subjects (skin roughness panel) judged from the skin surface microtopograph and state of peeling of the corneum as having a skin roughness evaluation of 1 or 2 based on the criteria shown in Table 3 and the lotions of Example 1 and Comparative Example 1 were applied two times a day half and half on the left and right of the face. After two weeks, replicas were once again taken and the state of the skin was examined and evaluated in the same way as mentioned above in accordance with the criteria shown in Table 5.

TABLE 5

Criteria for Evaluation of Skin Roughness

Score	Evaluation	Remarks
1	Disappearance of grooves and ridges peel-off of wide range of corneum	Rough skin
2	Unclear grooves and ridges, peel-off of corneum	↑
3	grooves and ridges are observed, but flat	
4	grooves and ridges are clear	↓
5	grooves and ridges are clear and well arranged	Beautiful skin

The judgement was made using the scores by the following criteria:

Good: Ratio of panel giving score of 4 and 5 at least 75%

Fair: Ratio of panel giving score of 4 and 5 from 25% to less than 75%

Poor: Ratio of panel giving score of 4 and 5 less than 25%

Example 2

A lotion composed of the composition of Table 6 was produced by a conventional method and evaluated in accordance with the above-mentioned method.

TABLE 6

Lotion

Component	Example 2
Erythritol	2.0%
Propylene glycol	1.0
Citric acid	0.2
95% ethanol	10.0
Perfume	q.s.
Hydrogenated lecithin	0.1
Polyoxyethylene (30) cholestanolether	0.1
Purified water	Balance
Effect of improvement of skin roughness	Good
Absorption into skin	Good

Comparative Example 3

A lotion composed of the composition of Table 7 was produced by a conventional method and evaluated in accordance with the above-mentioned method.

TABLE 7

Lotion

Component	Comparative Example 3
Glycerol	2.0%
Propylene glycol	1.0
Citric acid	0.2
95% ethanol	10.0
Perfume	q.s.
Purified water	Balance
Effect of improvement of skin roughness	Fair
Absorption into skin	Fair

As clear from the results of Tables 6 and 7, the external skin treatment composition of the present invention is a novel external skin treatment composition superior in the effect of improving of skin roughness and absorption into the skin.

Example 3: Nourishing Cream

A nourishing cream was produced by a conventional method in accordance with the following formula:

Component	% by weight
Stearic acid	2.0
Stearyl alcohol	7.0
Reduced lanolin	2.0
Squalane	5.0
Octyl dodecanol	6.0
Maltitol hydroxylaurylether	3.0
Glyceryl monostearate	2.0
Preservative	q.s.
Perfume	q.s.
Propylene glycol	5.0
Erythritol	2.0
Hydrogenated lecithin	0.5
Polyoxyethylene (30) cholestanolether	0.5
Potassium hydroxide	0.2
Purified water	Balance

Example 4: Emulsion

An emulsion was produced by a conventional method in accordance with the following formula:

Component	% by weight
Stearic acid	2.0
Cetanol	1.0
Vaseline	3.0
Lanolin alcohol	2.0
Liquid paraffin	8.0
Squalane	2.0
Octyl methoxycinnamate	2.0
Erythritol	10.0
Hydrogenated lecithin	0.5
Polyoxyethylene (30) cholestanolether	0.5
Polyoxyethylene (10) monooleate	2.5
Triethanol amine	1.0
Propylene glycol	5.0
Preservative	q.s.
Perfume	q.s.
Purified water	Balance

Example 5: Rinse-Off Mask

A rinse-off mask was produced by a conventional method in accordance with the following formula:

Component	% by weight
Glycerol	5.0
Dipropylene glycol	20.0
Ethanol	5.0
Carboxyvinyl polymer	1.0
Erythritol	5.0
Hydrogenated lecithin	0.1
Polyoxyethylene (30) cholestanolether	0.1
Polyethylene powder	3.0
Potassium hydroxide	0.4
Preservative	q.s.
Perfume	q.s.
Purified water	Balance

The external skin treatment compositions of Examples 2 to 5 were those with the effect of preventing skin roughness and improving skin toughness, quick in absorption into the skin, and superior in the moisturizing effect.

The external skin treatment composition of the present invention is an external skin treatment composition which

improves skin roughness, is quickly absorbed into the skin, and is superior in the moisturizing effect.

We claim:

1. A method for reducing the roughness of skin which comprises applying thereto an amount effective therefor of a composition selected from the group consisting of an aqueous solution, a solubilized composition, an emulsion, a powder, an oil-in-water composition, a gel, a two layer mixture of water and oil, a two-layer mixture of water and powder, and a three-layer mixture of water, oil and powder, each composition comprising 0.1 to 30% by weight of erythritol, 0.0001 to 0.5% by weight of hydrogenated lecithin, and 0.0001 to 0.5% by weight of a cholesterol which has been modified by a polvoxyethylene polyether.

2. A method as claimed in claim 1, wherein the number of moles of oxyethylene in the polyoxyethylene polyester is 5 to 70 moles per 1 mole of the cholesterol.

3. A method as claimed in claim 1, wherein the cholesterol which has been modified by a polyoxyethylene polyether is a polyoxyethylene (30) cholesterol ether having 30 moles of oxyethylene per 1 mole thereof.

4. A method as claimed in claim 1, wherein the content of the erythritol is 0.5 to 20% by weight, based on the weight of the external skin treatment composition.

5. A method as claimed in claim 1, wherein the content of the hydrogenated lecithin is 0.0005 to 0.5% by weight, based on the weight of the external skin treatment composition.

6. A method as claimed in claim 1, wherein the content of a cholesterol which has been modified by a polyoxyethylene polyether is 0.0005 to 0.5% by weight based on the weight of the external skin treatment composition.

7. A method of softening stratum corneum which comprises applying thereto an amount effective therefor of a composition selected from the group consisting of an aqueous solution, a solubilized composition, an emulsion, a powder, an oil-in-water composition, a gel, a two layer mixture of water and oil, a two-layer mixture of water and powder, and a three-layer mixture of water, oil and powder, each composition comprising 0.1 to 30% by weight of erythritol, 0.0001 to 0.5% by weight of hydrogenated lecithin, and 0.0001 to 0.5% by weight of a cholesterol which has been modified by a polyoxyethylene polyether.

8. A method as claimed in claim 7, wherein the number of moles of oxyethylene in the polyoxyethylene polyether is 5 to 70 moles per 1 mole of the cholesterol.

9. A method as claimed in claim 7, wherein the cholesterol which has been modified by a polyoxyethylene polyether is polyoxyethylene (30) cholesterol ether having 30 moles of oxyethylene per 1 mole thereof.

10. A method as claimed in claim 7, wherein the content of the erythritol is 0.5 to 20% by weight, based on the weight of the external skin treatment composition.

11. A method as claimed in claim 7, wherein the content of the hydrogenated lecithin is 0.0005 to 0.5% by weight, based on the weight of the external skin treatment composition.

12. A method as claimed in claim 7, wherein the content of a cholesterol which has been modified by a polyoxyethylene polyether is 0.0005 to 0.5% by weight based on the weight of the external skin treatment composition.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO : 5,753,242
DATED : May 19, 1998
INVENTOR(S): Fumiaki Nakamura, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title Page [56] "References Cited"	Before "5/94 Ziegler" delete "5310555" and insert --5310556--
Column 9, Claim 1, Line 14	After "Modified by a" delete "polvoxyethylene" and substitute --polyoxyethylene--
Column 9, Claim 2, Line 16	After "polyoxyethylene" and before "is 5" delete "polyester" and substitute --polyether--

Signed and Sealed this

Twenty-third Day of November, 1999

Attest:

Q. TODD DICKINSON

Attesting Officer

Acting Commissioner of Patents and Trademarks

US005466452A

United States Patent [19]

Whittle

[11] Patent Number: 5,466,452

[45] Date of Patent: Nov. 14, 1995

[54] **PHARMACEUTICAL COMPOSITIONS FOR THE TREATMENT OF SKIN DISORDERS**

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[21] Appl. No.: **108,640**

[22] PCT Filed: **Feb. 28, 1992**

[86] PCT No.: **PCT/GB92/00359**

§ 371 Date: **Aug. 26, 1993**

§ 102(e) Date: **Aug. 26, 1993**

[87] PCT Pub. No.: **WO/9215314**

PCT Pub. Date: **Sep. 17, 1992**

[30] **Foreign Application Priority Data**

Feb. 28, 1991 [GB] United Kingdom 9104286

[51] **Int. Cl.**[6] **A61K 35/78**

[52] **U.S. Cl.** **424/195.1**; 514/783; 514/858; 514/859; 514/860; 514/861; 514/862; 514/863; 514/864; 514/865

[58] **Field of Search** 424/195.1; 514/858–865

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Primary Examiner—Douglas W. Robinson
Assistant Examiner—Howard C. Lee
Attorney, Agent, or Firm—Bacon & Thomas

[57] **ABSTRACT**

A process is provided which is suitable for the preparation of herbal compositions for the treatment of skin disorders such as eczema and psoriasis. The process comprises preparing an extract or extracts of herbs which provide an anti-inflammatory agent, an adrenocortical stimulant and a cortisol protecting agent by steam distillation and decoction and then treating the extracts to reduce the polysaccharide and/or sugar content. This is achieved by fermentation or enzymic action or by extraction with a solvent having a polarity in the range E° 0.4 to 0.95 or by precipitation with an inorganic compound and/or colloid or by a combination of two or more of the above. As a final concentration step, the material is further purified by extraction with a solvent having a polarity in the range mentioned above. The reduction of the sugar/polysaccharide content greatly improves the handling characteristics of the extract which can be dried to a free flowing powder. Tablets and capsules for oral administration can be prepared from the extract and it is also suitable for the preparation of topical compositions.

24 Claims, No Drawings

PHARMACEUTICAL COMPOSITIONS FOR THE TREATMENT OF SKIN DISORDERS

The present invention relates to extracts of herbal compositions for use in the treatment of skin disorders such as, for example eczema and psoriasis and to processes for their preparation.

The etiology of eczema and psoriasis is not completely understood. However the symptomotology which characterizes the conditions is well described. The most important features are:

inflammation and pruritus (itching) which leads to a cycle of further irritation, inflammation and itching.

Eczema and psoriasis are expressions of an inappropriate immunological response whereby the body reacts to some of its tissue components as though they were foreign. Treatment is directed towards diminishing the severity of the immune response and alleviating symptoms. In conventional Western medicine topical corticosteroids are used to reduce inflammation and to suppress the immune response. Emollients are used to physically protect and smooth the skin and, where the skin is infected, antiobiotics are used.

Practitioners in traditional Chinese medicine however use decoctions of herbs for oral and topical treatment of dermatological conditions including eczema and psoriasis. A wide variety of agents have been used and in traditional Chinese medicine it is conventional to use a compound prescription which is designed by the practitioner after careful examination of the individual patient. It has been found by clinical experimentation that mixtures of certain herbs can be used to provide a composition which is effective in a large proportion of patients suffering from eczema and psoriasis, without recourse to individualisation of treatment. Different formulae have been devised for dry, weeping, infected and lichenified eczema although the mode of action of traditional Chinese medicines is not fully understood.

Table I shows a number of Chinese herbs which are traditionally used for the treatment of skin disorders together with the principle constituents and their pharmacological actions (Chang and But; Pharmacology and Applications of Chinese Materia Media. World Scientific Publishing 1986, Volumes I and II). The table shows that many of the agents traditionally used have pharmacological properties which are appropriate for the treatment of symptoms of eczema and psoriasis, namely anti-inflammatory, analgesic, anti-pyretic, anti-pruritic, anti-bacterial and immune suppressent activity. Some of the agents listed may stimulate the adrenal cortex to produce endogenous corticosteroids and others may inhibit the breakdown of cortisol in certain tissues such as the skin and lung. The combination of herbs to provide a combined attack on the symptoms of eczema and psoriasis are therefore rational even though at present it is not known exactly which of the constituents are responsible for the beneficial therapeutic effects of the mixtures.

It is possible that some of the herbs in the mixtures are necessary in order to increase the solubility of some of the active constituents in water since the traditional method of preparing extracts is by decoction i.e. boiling in water. In traditional Chinese medicine some herbs are included in prescriptions because they act as demulcents i.e. agents which have a soothing effect on the gastrointestinal tract and facilitate patient acceptance. It is firmly believed by traditional Chinese practitioners that the toxicity of mixtures of herbs is less than that of the herbs given in isolation. Although this has yet to be rigorously proved in controlled clinical trials, conventional wisdom indicates that some of the herbal components have biological activities which

summate, and others antagonise the toxic effect of active components. Until the active components have been identified with certainty it has proved prudent to use a decoction, extract or fractionated extract of a plurality of herbs. To be useful in practice it is necessary to have one or more fixed composition mixtures. Surprisingly, it has been found that fixed combinations of specific herbs can be used to treat different types of eczema and psoriasis.

For example a particularly useful formulation of 10 herbs which has been found to be effective in the treatment of dry ("red all over") childhood eczema can be prepared by adding about 300 ml of water to every 38.75 g of herb contained in a (non-aluminium) saucepan, bringing to the boil and simmering for one and a half hours. During this process the volume of liquid is reduced until a volume of about 50 ml per 38.75 g of original herb is obtained. The final volume of the decoction is not critical and when removed from the exhausted herbs can be diluted to taste. The decoction obtained from the herbs is prepared fresh each day. Some of the herbs contain volatile oil and these herbs are added three minutes before the end of the decoction period to minimise loss of volatile oil.

The process of decoction is efficient in the extraction of the active principals but additionally a large quantity of inactive material in the form of polysaccharides, colouring matter, sugars and tannins is also extracted. There is therefore a need for a method of preparing herbal extracts which are more concentrated in respect of the active ingredients and contain much lower amounts of extraneous material than those extracts hitherto known.

The present inventors have devised a method by which this might be achieved which allows a smaller dosage unit to be administered.

Thus a process for the preparation of a composition for treating skin disorders in accordance with the invention comprises:

(a) preparing an extract or extracts of a plurality of herbs, the herbs being such as to provide an anti-inflammatory agent, an adrenocortical stimulant and a cortisol-protecting agent by subjecting said herbs to steam distillation and decoction,

(b) reducing the amount of polysaccharides and/or sugars in at least a proportion of the extract or extracts to less than 5% by weight under conditions which do not substantially reduce the content of glycosides which are present in said material by one or more of:

(i) fermentation or enzymatic action,

(ii) extraction with a solvent having a polarity in the range E^o 0.4 to 0.99 or a mixture of solvents at least one of which has a polarity in said range,

(iii) precipitation with an inorganic compound and/or a colloid, and

(c) concentrating the active agents present in the extracted material by further extraction with a solvent having a polarity in the range E^o 0.4 to 0.99 or a mixture of solvents at least one of which has a polarity in said range.

The preparation of an extract in step (a) of the above method is advantageously carried out by the traditional decoction process of boiling the herbs in water. Prior to decoction any volatile oils or other volatile components can be removed from the herbs by steam distillation and retained for re-introduction into the final extract if desired. These volatile components can be particularly useful in the formulation of treatments for eczema and psoriasis.

The reduction of the polysaccharides and/or sugar carried out in step (b) is extremely important in the process of the

invention. Extracts containing substantial amounts of sugars are very difficult to evaporate to a free flowing powder and often nothing more than a solid sticky mass can be achieved. Preferably the amount of polysaccharides and/or sugars is reduced to less than 2.5% and more preferably less than 5% by weight. It is also important that the step for reducing excess polysaccharides and sugars is carried out under conditions which do not substantially reduce the glycoside content since one or more of the active agents may be a glycoside.

Where the polysaccharide and/or sugar content is to be reduced by fermentation it is preferable to incubate the total water extraction from the decoction prepared in step (a) with barley malt or with a yeast such as saccharomyces cerevisiae or a fungus such as *Aspergillus oryzae* or other microorganism providing amylase and/or saccharolytic enzymes. Isolated and purified amylolytic or saccharomytic enzymes may also be used, optionally bound to a membrane or other support. Where these enzymes will also split glycosides it is preferable to use an inhibitor of glycosidase.

In a fermentation process ethyl alcohol may be formed in situ and may be used in a further separation of active ingredients.

If the polysaccharide and/or sugar content is to be reduced by the further extraction of the initial extract with a solvent or mixture of solvents at least one of which has a polarity in the range E° 0.4 to 0.99 it is preferable if the solvent is one or more of chloroform, methylene chloride, ethyl acetate, tetrahydrofuran, methylethylketone, acetone, acetonitrile, propanol, ethanol, methanol, industrial methylated spirits or a not less than 70% solution of one or more of the above in water. Particularly preferred are 70% solutions of ethanol, propanol or industrial methylated spirits.

The addition of these solvents results in a fractional precipitation of polysaccharide and/or sugars, the desired active components remaining in solution.

As an alternative to, or as well as fermentation, enzymic treatment and/or solvent extraction in step (b) the polysaccharide and/or sugar content can be reduced by precipitation with an inorganic compound and/or a colloid. A preferable inorganic compound for use is calcium hydroxide.

After the sugar reducing step a further concentration of the extract is generally required. In particular it is desirable to substantially rid the extract of polyphenyls and tannins. In the process of the invention this is achieved by the further extraction step (c) using a solvent or mixture of solvents at least one of which has a polarity in the range E° 0.4 to 0.99. Suitable solvents may be selected from the list given above in connection with step b(ii).

The extract produced by the process of the invention may be evaporated to a paste, mixed with excipients and extruded to granules for oral administration, optionally with the addition of flavourings.

The extract prepared may be diluted in an aqueous solution for oral administration. The invention particularly provides compositions containing the herbal extract made by the process of the invention containing an anti-inflammatory agent, an adrenocorticol stimulant and a cortisol protecting agent which is admixed with a pharmaceutically suitable excipient, diluent or carrier many examples of which are well known to the man skilled in the art. A particularly useful carrier is silica gel.

For example the composition may be prepared for topical administration using well established formulations which produce an emollient ointment or water dispensable cream. The composition may also be prepared in a unit dosage form such as a tablet or capsule for oral administration. For such use it is advantageous if after the final extraction step the herbal extract is processed to form a powder, for example by spray drying, freeze drying or evaporation.

Chinese medicine teaches that substantially all of the herbs in a composition are necessary for activity and that the herbs are best given in extemporaneously prepared decoction. However it has now surprisingly been found that the anti-eczema activity of the composite herbal preparation resides mainly, if not exclusively in a restricted number of herbs. It is therefore possible to reduce the amount of unnecessary material from the composition by limiting the number of herbs used, and to then further reduce the quantity of material given by preparing a composition in concentrated form in accordance with the invention wherein extraneous materials are removed.

Herbs selected from the list in Table I are suitable for use in the invention and a particularly preferred composition is one containing extracts from *Rehmannia glutinosa, Dictamnus augustifolia, Glycyrrhiza uralensis* and either *Ledebouriella sesloides* or *Schizonepeta tenuifolia.* Optionally Tribulus terrestris can be included. Another preferred composition is one containing the first 10 herbs listed in Table I.

It is preferable if one of the herbs included in the mixture provides an anti-pruritic (anti-itching) agent. As some of the herbs may have a bitter taste it is also preferable to add a sweetening agent for oral compositions.

The herbal extract may be prepared in accordance with the invention either by carrying out steps (a), (b) and (c) on a plurality of herbs which are first mixed together or by carrying out steps (a), (b), (c) on some or all of the individual herbs and mixing together the final extracts.

A disadvantage of the former method is that the yield of active ingredient from each herb varies from batch to batch so that the final concentration of each active agent in the mixture will not be known. By preparing separate extracts of each herb and then later mixing them, each may be assayed using a marker substance which assists in standardizing the dose given to the patient. A further advantage is that full processing for sugar reduction need only be carried out on those herbs in the mixture having a high polysaccharide or sugar/content which makes them difficult to handle.

The invention is now illustrated in the following non-limiting examples.

Example 1

The following ingredients are coarsely chopped or powdered and volatile oil is removed by steam distillation:

	Weight in Grams
Radix Ledebouriellae	112.5
Fructus Tribuli	112.5
Caulis Akebiae	112.5
Radix Rehmanniae (raw)	168.75
Radix Glycyrrhizae	56.25
Radix Paeonia rub.	112.5
Cortex Dictamni	168.75
Moutan radicis	112.5
Gypsum Fibrosum	450.0
Artemisia scopariae	112.5

The oil is reserved and the residue is mixed with one litre of water, boiled for one and a half hours and allowed to cool to a temperature of 35° C. to form a decoction.

100 ml of an actively growing culture of fresh baker yeast is added to the mixture of herbs and water and maintained

with stirring for 8 hours or until the sugar content of an aliquot is less than 0.4%.

The vegetable matter is removed by straining and yeast is removed from the liquor by centrifugation. The filtered liquid is evaporated to dryness.

The extract thus prepared is stirred with 200 ml of ethyl acetate for 10 minutes, separated by centrifugation and the solution reserved. A further quantity of 50 ml ethyl acetate is added, the mixture, stirred and separated. The combined filtrate is evaporated to dryness.

The reserved oil is added back. The resulting product is a brown extract which is free flowing and can be used, with suitable flavourings, as the dosage form. It can be formulated into conventional pharmaceutical dosage forms, with addition of excipients, for the treatment of dry eczema. The quality given above is sufficient for 10 days treatment of an adult.

Example 2

The following herbs are coarsely chopped or powdered and decocted with 4 litres of water for 1 hour:

	Weight in Grams
Radix Rehmanniae (raw)	168.75
Radix Paeonia rubra	112.50
Radix Glycyrrhizae	56.25
Cortex Dictamni radicis	168.75
Rhizoma Smilacis glabrae	168.75
Fructus Kochiae	56.25
Radix Angelica sinensis	112.50
Semen Sesami (black)	168.75

The liquor is removed by centrifugation. The extract is then evaporated until it contains 50% solids w/v and 10% by weight calcium hydroxide is added. Three volumes of isopropanol are added with mixing and the mixture allowed to stand at room temperature. The clear supernatant is removed, 1 volume of 75% isopropanol added, mixed and the residue centrifuged. The pooled supernatants are evaporated to dryness. The resulting refined extract can be mixed with pharmaceutical aids and filled into capsules or compressed into tablets.

Example 3

An extract containing the following herbs is prepared:

	Weight in Grams
Ledebouriella sesloides	10
Paeonia rubra	12
Rehmannia glutinosa	10
Glycyrrhiza uralenis	15

For the herbs *Ledebouriella sesloides* and *Paeoniae rubra* a decoction is prepared of each of the herbs individually by boiling in successive quantities of water until complete exhaustion of the marc. The extracts are dried.

Extracts of each of the herbs *Rehmannia glutinosa* and *Glycyrrhiza uralenis* are prepared by the method of Example 2. The dried extracts of all four herbs are combined in the weights shown above which provides an adult daily dose for the treatment of eczema.

Example 4

An extract is prepared from a mixture of the following herbs using the method described in Example 2:

	Weight in Grams
Radix Rehmanniae (raw)	90
Rhizoma Smilacis glabrae	90
Radix Glycyrrhizae	30
Cortex Dictamni Radicis	90
Radix Paeonia Rub	60
Radix Artemisia scopariae	60
Fructus Kochiae	30
Sophora flavescens	20
Rhizoma atractyloides	60

The composition is suitable for treatment of chronic, lichenified, "weeping" eczema, and the quanities given are suitable for 10 days treatment of an adult patient.

Example 5

An extract is prepared from a mixture of the following herbs using the method described in Example 2:

	Weight in Grams
Rhizoma Similacis glabrae	300
Cortex Dictamni Radicis	100
Radix Clematidis	100
Radix Angelica sinensis	100
Radix Polygonum multiflora	100
Radix Salvia miltiorrhiza	100
Rhizoma Ligustiae chuanxiong	100

The composition is suitable for treatment of "stable" psoriasis and the quanitites given are suitable for 10 days treatment of an adult patient.

Example 6

An extract is prepared from a mixture of the following herbs using the method described in Example 2:

	Weight in Grams
Rhizoma Smilacis glabrae	300
Cortex Dictamni Radicis	100
Radix Clematidis	100
Radix Rhemanniae	200
Rhizona Imperata cylindrica	100
Radix Arnebiae (Ser) *lithospermum*	10
Radix Salvia miltiorrhiza	10
Radix Ligustiae chuanxiong	10
Carthamus tinctorus	10

The composition is suitable for the treatment of progressive psoriasis and the quantities given above are suitable for 10 days treatment of an adult patient.

Example 7

A refined extract is prepared according to the method given in Example 2 from the following herbs and then mixed with an emulsifying ointment base to produce an oil/water cream:

Phellodendron anurense (extract from 20 g herb)

Scutellaria baicalensis (extract from 20 g herb)

Coptis chinensis (extract from 20 g herb)

Cetomacrogol Emulsifying Ointment to 100 g

Example 8

A refined extract is prepared according to the method given in Example 2 from *Sophora flavescens*, and incorporated in an emulsifying ointment base according to the following formula:

Sophora flavescens	(extract from 20 g herb)
Emulsifying wax	30 g
Hard paraffin	5 g
Cod liver oil	15 g
Evening Primrose Oil	15 g
White Soft Paraffin to	100 g

This ointment can be applied thinly to the skin or can be mixed with water to produce an oil in water emollient cream.

Example 9

A refined extract prepared according to the method given in Example 2 from *Rheum palmatum* is incorporated in an emulsifying ointment base:

Rheum Palmatum (extract from 30 g herb)

Cetomacrogol Emulsifying Ointment to 100 g

In this example and in Examples 7 and 8 the quantity of extract of herb is illustrative and not limited to the proportions given.

Example 10

A decoction was prepared using the method given in Example 1 from 38.75 g of the herbs listed in that Example to give a final volume of 50 ml. Using a proprietary test kit, approximate dilutions of the decoction were tested for sugar before, and at intervals after adding 3 ml of a fresh 10% yeast suspension to the decoction. The mixture was incubated at 30° C. with occasional stirring.

Time (h)	Approx concentration of sugar as tested	Dilution	Concentration in decoction by weight
0	>0.2%	1:300	>30%
½	0.2–0.4%	1:50	10–20%
1	0.2–0.4%	1:10	2–4
2	0.2–0.4%	1:1	0.2–0.4%

*Limit of detection of glucose oxidase test kit.

After fermentation, the decoction is markedly less sweet although there is residual sweetness contributed by the liquorice contained in the mixture. When the resulting solution is filtered and evaporated to dryness 4.7 g of extract is produced. Example 11

The following herbs are coarsely chopped and volatile oil is removed by steam distillation:

	Weight in Grams
Radix ledebouriellae	300
Fructus Tribuli	300
Lacca	450
Caulis Akebiae	300
Radix glycyrrhizae	150
Radix Rehmanniae (raw)	450
Radix Paeonia rubra	300
Herba Lophatheri	300
Cortex Dictamni radicis	450
Herba Schizonepetae	150
	3100 g

The oil is reserved and the residue is mixed with one litre of water, boiled for one and a half hours and allowed to cool to a temperature of 35° C. to form a decoction.

100 ml of an actively growing culture of fresh bakers yeast is added to the mixture of herbs and water and maintained with stirring for 8 hours or until the sugar content of an aliquot is less than 0.4%.

The vegetable matter is removed by straining and yeast is removed from the liquor by centrifugation. The filtered liquid is evaporated to dryness.

The extract thus prepared is stirred with 200 ml of 70% industrial methylated spirits for 10 minutes, separated by centrifugation and the solution reserved. A further quantity of 50 ml 70% industrial methylated spirits is added, the mixture stirred and separated. The combined filtrate is evaporated to a syrupy consistancy. Weight per ml is determined and ⅓ of this weight of colloidal silica added, and the extract evaporated to dryness.

The resulting dry extract is a brown extract which is free flowing and can be used, with suitable flavourings, as the dosage form as powder, granules, capsules or tablets, for the treatment of dry eczema. These quantities are sufficient for 20 days treatment for an adult.

TABLE I

CHINESE PLANT NAME	LATIN NAME	CONSTITUENTS	PHARMACOLOGY	TRADITIONAL USE IN CHINA
Bai Tai Weng	*Potentilla chinensis*	triterpenoid seponins	Antibacterial, anti-trichomonal, anti-amoebic	Bacillary dysentery, amoebic dysentery, lymph node TB, Squamous cell cancer
Dihuang	*Rehmannia glutinosa* (Libosch) (Scrophulatiaceae)	β-sitosterol, mannitol, stigmasterol, campesterol, catalpol, rehmannin, vitamin A	Reduction of cortisol, diuretic, anti-inflammatory, anti-fungal	Immunological diseases, infectious hepatitis, hypertension, neurodermatitis
Chi Shao	*Radix paeoniae*	paeoniflorin,	Vasodilator. Increases	Pain in chest, pain in

TABLE I-continued

CHINESE PLANT NAME	LATIN NAME	CONSTITUENTS	PHARMACOLOGY	TRADITIONAL USE IN CHINA
	lactiflora/veitchii (Ranunculaceae)	albiflorin, oxypaeoniflorin, benzoylpaeoniflorin, benzoic acid, tannin	coronary blood flow, increases myocardial oxygen, inhibits platelet aggregation, sedative, analgesic, antispasmodic, anti-inflammatory	abdomen, dysmenorrhoea, amenorrhoea, carbuncle, epistaxis, conjunctival congestion, traumatic injury
Bai Xan Pi	*Dictamnus augustifolia* Chinese Dittany Root bark + (Rutaceae)	Dictamnine, dictamnolactone, sitosterol, obacunic acid, trigonelline, choline campesterol, fraxinellon shimmianine fagarine, dasycarpamine	Cardiotonic, antifungal, smooth muscle stimulant, antipyretic, shortened clotting time (iv)	Anti-rheumatic, anti-inflammatory, pityriasi8 rosea, scabies, dermatomycoses, prurigo, rheumatic pain, jaundice
Gan Cao	*Glycyrrhiza uralensis* (Fisch) Licorice (Leguminosae)	Triterpenes (glycyrrhizin 'G' etc) Flavonoids (liquiritin etc) Berniarin, umbelliferone, ferulic acid, sinapic acid etc.	Adrenocorticomimetic, anti-inflammatory, anti-ulcer, antispasmodic, detoxicant	Addisons Disease, gastric & duodenal ulcer, pulmonary TB, infectious hepatitis, eye inflammatory disease, purpina
Fang Feng	*Ledebouriella sesloides*	Volatile oil, mannitol, bitter glycosides, phenolic glycosides, polysaccharides, organic acids	Anti-inflammatory, analgesic, antipyretic, anti-convulsant, antimicrobial	Rosacea, common cold, elimination of heavy metals, pnnitus, urticaria
Ci Ji Li (Bai Ji Li)	*Tribulus terrestrial/Fructus tribuli*	Diosgenin, ruscogenin, hecogenin, tribuloside, kaempferol, rutoside, astragalin, harmine	Hypotensive effect on smooth muscle, diuretic, cough suppressant	Headache, dizziness, red eye, itching, chest
Dan Zhu Ye	*Lopatheri gracile*	Arundoin, cylindrin, friedelin, taraxerol, β-sitosterol	Antibacterial, diuretic, antipyretic	Febrile disease, stomatitis swelling & pain in gingivae, urethral inflammation and pain
Jing Jie Sui	*Schizonepeta tenuifolia*	d-menthone, l-pulegone, schizoneptosides A & B d-limone	Antipyretic, antibacterial, anti-inflammatory, analgesic, aniitubercular	Influenza fever, headache, sore throat, measles, urticaria
Mu Tong	*Akebia trifoliata*	Akebin which hydrolyses to hederagenin, oleandic acid, rhamnose & glucose	Diuretic, cardiotonic, stimulation of GI tract smooth muscle, uterine SM relaxant, antifungal	Urinary infections, oedemia, amenorrhoea, diarrhoea, period pain, prelapse uterus
Lei Gong Teng	*Trypterigium wilfordii*	Wilfordine, and related alkaloids, celacemine and other macrocyclic alkaloids, triptolide and other epoxyditerpenes, celastol and other triterpenes	Anti-inflammatory, antineoplastic, immunosuppressant, insecticide	Anthelmintic, anti-inflammatory, anti-rheumatic
Ku Shen	*Sophora flavescens*	Matrine, oxymatrine, sophoranol, flavonoids, cytosine	Diuretic, antineoplastic, immunosuppressant, bradycardia, reduced myocardial contractility, hypotensive, bronchodilator, anti-microbial	Anthelmintic, anti-inflammatory, jaundice, scabies, enteritis, dysentery
Bei Yin Chen	*Artemesia scopariae*	Volatile oil, cholorogenic acid, caffeic acid, capillarisin, methylcapillarisin, phenoxychromones, flavonoids	Antipyretic, cholagogue, hepatoprotective, antilipidaemic, hypotensive, antibacterial	Jaundice, hepatitis
Mu Dan Pi (Moutan)	*Paeonia suffructicosa*	Paeonol, paeonoside, paconolide, paeoniflorin, volatile oil, phytosterol	Antimicrobial, anti-inflammatory, hypotensive analgesic	Convulsions, ulcers, fractures, concussion, sprains
Zhi Mu	*Anemarrhena asphodeloids*	Saponins, sarsasapogenin,	Adrenocortical stimulation,	Dry cough, fever

TABLE I-continued

CHINESE PLANT NAME	LATIN NAME	CONSTITUENTS	PHARMACOLOGY	TRADITIONAL USE IN CHINA
		markogenin, neogitogenin, chimonin, isomangiferin	hypoglycaemic, antibacterial	
Dang Gui	*Angelica sinensis*	Volatile oil, ligustilide, butylidenephthalide, butanedioic acid, angelicane, β-sitosterol, vitamins B_{12}, A & E, nicotinic acid, folic acid, ferulic acid, succinic acid	Immunosuppressant, anti-inflammatory, uterine relaxant, hypotensive, anti-platelet aggregation, antilipidaemic	Dysmenorrhea, anaemic, amenorrhoea, headache, constipation, rheumatism
Zi Cao	*Lithospermum erythrorhizon*	Acetylshikonin, β-, dimethylactylalkannin shikonin	Antineoplastic, antipyretic	Fever, eczema
Di Fu Zi	*Kochia scopariae*	Kochiasides	Anti-inflammatory	Eczema, pruritus, rheumatism
Tu Fu Ling	*Smilacis Glabrae*	Sarsagogenin, triterpene, glycosides	Immunosuppressant, anti-inflammatory	Eczema, leukorrhea, lymphedema, muscle cramp
Chuan Xiong	Rh. *Ligusticum chuanxiong*	Volatile oil, alkaloids, phenolic compounds, Lactones	β-agonist, coronary dilator, peripheral dilator, vasodilators, inhibition of platelet aggregation	Analgesic, rheumatism, sores, ulcers, dysmenorrhoea
Dan Shen	*Salvia miltiorrhiza*	Tanshinones I, IIa, IIb, miltirone, isotanshinones, salviol etc.	Improvement of circulation	Angina, pectoris, amenorrhoea, dysmenorrhoea, fractures, sprains, insomnia
He Shou Wu	*Polygonum multiform*	Anthraquinone, glycosides & aglycones	β-blocker, lipid-lowering, antibacterial	Tinnitus, weakness of lower back, constipation
Bai Mao Gen	*Imperata cylindrica*	Cyclindrin, arunoin, ferneol	Diuretic, coagulant	Urinary tract infection, oedema, jaundice
Hong Hua	*Carthamus tinctorius*	Dihydroflavone, glycosides	Cardiotonic	Amenorrhoea, dysmenorrhoea, fractures, concussion, sprains
Cang Zhu	*Atratylodes chinensis*	β-eudesmol, hinesol, atractylodin	Antiseptic. Hypoglycaemic, diuretic, gastritis, antispasmodic	Rheumatism, oedema, diarrhoea, abdominal distention
Wei Ling Xian	*Clematis chinensis*	protoanemonin, anemonol, sterols, saponins	Antihistaminic, antibacterial, induction of labour, vasodilator	Rheumatism, arthritis, numbness of limbs, traumatic injury, psoriasis
Huang Bo	*Phellandendron amurense*	berberine, phellandendrine, magnoflorine, palmatine, obakulactone, obakunone	Anti-micobial Hypotensive muscle relaxant	Decongestant
Huang Qin	*Scutellaria baicalensis*	β-sitosterol, benzoic acid, baicalein, baicalin, wogonin, wogonoside	Anti-microbial, sedative, antipyretic, hypotensive, anti-inflammatory, diuretic, anti-cholinergic	Fever, cough, pneumonia, jaundice, hepatitis, dysentery. conjunctivitis, hypertension
Huang Lian	*Coptis chinensis*	berberine, coptisine, worenine and other alkaloids	Antimicrobial, anti-cholinergic, hypotensive, muscle relaxant	Nausea, vomiting, dysentery, enteritis, conjunctivitis, otitis media
Da Huang	*Rheum palmatum*	anthraquinones, glycosides, sennosides tannins	Cathartic action, antispasmodic, choloretic action	Indigestion, jaundice, amenorrhoea, burns and scalds

Glossary of Terms

The terms used define the identity of the plant or ingredient are given in the examples as Latin binomial names. The parts of the plant used are defined as follows:

Caulis -	Stem
Cortex -	Bark
Cortex radicis -	Root Bark
Herba -	Aerial parts
Fructus -	Fruit

-continued

Radix -	Root
Rhizoma -	Rhizome
Semen -	Seed
Spika -	Flowering spike

I claim:

1. A process to make a composition for treating eczema, psoriasis, pruritis and inflammatory reactions of the skin which comprises:

(a) subjecting a plurality of herbs having anti-inflammatory activity, adrenocortical stimulating activity and corticosol-protecting activity to steam distillation and decoction, to produce an extract of the herbs;

(b) reducing the amount of polysaccharides and/or sugars, in the extract to less than 5% by weight under conditions which do not substantially reduce the content of glycosides which are present in said material by one or more of:

(i) fermenting with barley malt or with a microorganism which produces amylase and/or saccharolytic enzymes or by using isolated amyolytic or saccharolytic enzymes,

(ii) extracting with a solvent having a polarity in the range E° 0.4 to 0.99, or a mixture of solvents at least one of which has a polarity within said range,

(iii) precipitating the polysaccharide and/or sugar with an inorganic compound; and

(c) concentrating the active agents present in the extracted material by further extracting with a solvent having a polarity in the range E° 0.4 to 0.99, or a mixture of solvents, at least one of which has a polarity within said range,

wherein the herbs are selected from the group consisting of *Potentilla chinensis* (Bai Tai Weng), *Rehmannia glutinosa* (Dihuang), *Radix paeoniae lactiflorae/veitchii* (Chi Shao), *Dictamnus augustifolia* (Bai Xan Pi), *Glycyrrhiza uralensis* (Gan Cao), *Ledebouriella sesloides* (Fang Feng), *Tribulus terrestris* (Ci Ji Li), *Lopatheri gracile* (Dan Zhu Ye), *Schizonepeta tenuifolia* (Jing Jie Sui), and *Akebia trifoliata* (Mu Tong).

2. A process as claimed in claim 1 wherein the microorganism used in step b(i) is *Saccharomyces cerevisiae* or *Aspergillus oryzae*.

3. A process as claimed in claim 1 wherein the isolated amylolytic or saccharolytic enzymes used in step b(i) are used in the presence of an inhibitor of glycosidase.

4. A process as claimed in claim 1 wherein the isolated amylolytic or saccharolytic enzymes used in step b(i) are bound to a support.

5. A process as claimed in claim 4 wherein the support is a membrane.

6. A process as claimed in claim 1 wherein, when the polysaccharide content or sugar content, or both, is reduced by the solvent extraction of the active agents in the method of step b(ii), the solvent is selected from the group consisting of chloroform, methylene chloride, ethyl acetate, tetrahydrofuran, methylethylketone, acetone, acetonitrile, propanol, ethanol, methanol and industrial methylated spirits.

7. A process as claimed in claim 1 wherein, when the polysaccharide content and/or sugar content is reduced by the solvent extraction of the active agent in the method of step b(ii) the solvent used is a 70% or greater solution in water of a solvent selected from the group consisting of chloroform, methylene chloride, ethyl acetate, tetrahydrofuran, methylethylketone, acetone, acetonitrile, propanol, ethanol, methanol and industrial methylated spirits.

8. A process as claimed in claim 1 wherein, when the polysaccharide content and/or sugar content is reduced by the precipitation method of step b(iii), the inorganic compound is a colloid.

9. A process as claimed in claim 1 wherein when the polysaccharide content and/or sugar content is reduced by the precipitation method of step b(iii), the inorganic compound is calcium hydroxide.

10. A process as claimed in claim 1 wherein in the solvent extraction method of step (c), the solvent is selected from the group consisting of chloroform, methylene chloride, ethyl acetate, tetrahydrofuran, methylethylketone, acetone, acetonitrile, propanol, ethanol, methanol and industrial methylated spirits.

11. A process as claimed in claim 1 wherein in the solvent extraction method of step (c), the solvent used is a 70% or greater solution in water of a solvent selected from the group consisting of chloroform, methylene chloride, ethyl acetate, tetrahydrofuran, methylketone, acetone, acetonitrile, propanol, ethanol, methanol and industrial methylated spirits.

12. A process as claimed in claim 10 wherein tannins and polyphenyls are removed from the extracted material.

13. A process as claimed in claim 1 wherein volatile oils and other volatile components which are removed during steam distillation are retained and reintroduced into the composition.

14. A process as claimed in claim 1 which further comprises drying the concentrated extract to powder form.

15. A process as claimed in claim 14 wherein drying is effected by evaporating, spray drying or freeze drying.

16. A process as claimed in claim 1 wherein the herbal extract from step (c) is dried to a paste, mixed with excipients and extruded to form granules.

17. A herbal extract for treating skin disease comprising an anti-inflammatory agent, an adrenocortical stimulant and a cortisol-protecting agent when produced by a process as claimed in claim 1.

18. An extract as claimed in claim 17 when admixed with a pharmaceutical excipient, diluent or carrier.

19. An extract as claimed in claim 18 wherein the carrier is silica gel.

20. An extract as claimed in claim 17 which is prepared in unit dosage form.

21. An extract as claimed in claim 17 which is in the form of an aqueous solution.

22. An extract as claimed in claim 17 which is in the form of an ointment or cream.

23. A process as claimed in claim 1 wherein the composition comprises:

(a) *Rehmannia glutinosa* as a cortisol-protecting agent and adrenocortical stimulant;

(b) *Dictamnus augustifolia* as an alkaloid component,

(c) *Glycyrrhiza uralensis* as an adrenocortical stimulant, and

(d) *Ledebouriella sesloides* or *Schizonepeta tenuifolia* as an anti-inflammatory agent.

24. A process as claimed in claim 23 wherein the composition further comprise *Tribulus terrestris*.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 5,466,452

DATED : November 14, 1995

INVENTOR(S) : WHITTLE

It is certified that error appears in the above-indentified patent and that said Letters Patent is hereby corrected as shown below:

Column 1, line 9, "symptomotology" should read --symptomatology--.

Column 1, line 13, before "of" delete the indentation.

Column 1, line 26, "have" should read --has--.

Column 1, line 39, "principle" should read --principal--.

Column 2, line 24, "principals" should read --principles--.

Column 3, line 14, "saccharomyces cerevisiae" should read --*Saccharomyces cerevisiae*--.

Column 3, line 21, "in" should read --*in*--.

Column 3, line 22, "situ" should read --*situ*--.

Column 4, line 19, "*augustifolia*" should read --*angustifolia*--.

Column 4, line 20, "Tribu-" should read --*Tribu*---.

Column 4, line 21, "lus terrestris" should read --*lus terrestris*--.

Column 4, in the table of Example 1, sixth entry "rub" should read --*rub.*--

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 5,466,452

DATED : November 14, 1995

INVENTOR(S) : WHITTLE

It is certified that error appears in the above-indentified patent and that said Letters Patent is hereby corrected as shown below:

Column 5, line 16, "days" should read --days'--.

Column 6, in the table of Example 4, fifth entry "rub." should read --*rub.*--

Column 6, line 19, "days" should read --days'--.

Column 6, in the table of Example 5, "*Radicis*" should read --*radicis*--.

Column 6, line 37, "quanitites" should read --quantities--.

Column 6, in the table of Example 6, "*Radicis*" should read --*radicis*--.

Column 6, line 59, "days" should read --days'--.

Column 7, line 28, "*Palmatum*" should read --*palmatum*--.

Column 7, in the table of Example 10, ">0.2%" should read -->0.2%*--.

Column 8, line 6, "is" should read --are-- and "Example 11" should be centered as a title on the next line.

Column 8, line 14, "*Tribuli*" should read --*tribuli*--.

Column 8, line 15, "Lacca" should read --*Lacca*--.

Column 8, line 28, "bakers" should read --baker's--.

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 5,466,452

DATED : November 14, 1995

INVENTOR(S) : WHITTLE

It is certified that error appears in the above-indentified patent and that said Letters Patent is hereby corrected as shown below:

Column 8, line 44, "consistancy" should read --consistency--.

Column 8, line 53, "days" should read --days'--.

Columns 9 and 10 (TABLE I-continued):

Column 2, row 2, "augustifolia" should read --*angustifolia*--.
Column 5, row 2, "pityriasi8" should read --pityriasis--.
Column 5, row 4, "pnnitus" should read --pruritus--.
Column 2, row 6, "Lopatheri" should read --*Lophatheri*--.
Column 4, row 7, "aniitubercular" should read --antitubercular--.
Column 5, row 8, "oedemia" should read --oedemtia--.
Column 5, row 8, "prelapse" should read --prolapsed--.

Column 11 and 12 (TABLE I-continued)

Column 5, row 2, "anaemic" should read --anaemia--.
Column 5, row 5, "leukorrhea" should read --leukorrhoea--.
Column 5, row 5, "lymphedema" should read --lymphoedema--.
Column 2, row 6, "Rh" should read --*Rh.*--.
Column 3, row 6, "Lactones" should read --lactones--.
Column 4, row 6, after "coronary" insert --vaso-- and after "peripheral" insert --vaso--.
Column 5, row 7, "Angina, pectoris" should read --Angina pectoris--.
Column 4, row 13, "Anti-micobial" should read --Anti-microbial--.
Column 4, row 14, "Hypotensive muscle" should read --Hypotensive, muscle--.

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 5,466,452

DATED : November 14, 1995

INVENTOR(S) : WHITTLE

It is certified that error appears in the above-indentified patent and that said Letters Patent is hereby corrected as shown below:

Column 11, line 61, "used define" should read --used to define--.

Column 12, line 64, "*Cortex radicis*" should read --Cortex radicis--.

Column 13, line 10, "pruritis" should read --pruritus--.

Column 13, line 38, "*augustifolia*" should read --*angustifolia*--.

Column 14, line 57, "*augustifolia*" should read --*angustifolia*--.

Column 14, line 63, "comprise" should read --comprises--.

Signed and Sealed this

Twenty-eighth Day of October, 1997

Attest:

BRUCE LEHMAN

Attesting Officer

Commissioner of Patents and Trademarks